

PATENT

U.S. Appln. Ser. No.: **09/402,618**
Attorney Docket No. **FORS-04012**

beginning on page 2 of this communication. A marked-up version of the rewritten, added, and/or cancelled claims pursuant to 37 C.F.R. §1.121 (c)(1)(ii) is attached as Appendix 1. A clean version of the entire set of pending claims pursuant to 37 C.F.R. §1.121 (c)(3) as they would appear following entry of this amendment is attached as Appendix 2.

Please substitute the following Claims for the previously pending Claims:

C1 90. A method, comprising:

- a) providing:
 - i) target nucleic acid comprising first and second non-contiguous single-stranded regions separated by an intervening region comprising a double-stranded region, wherein said target nucleic comprises at least a portion of Hepatitis C virus nucleic acid;
 - ii) a bridging oligonucleotide capable of binding to said first and second non-contiguous single-stranded regions;
 - iii) a second oligonucleotide capable of binding to a portion of said first non-contiguous single-stranded region; and
 - iii) a cleavage agent;

C2 b) mixing said target nucleic acid, said bridging oligonucleotide, said second oligonucleotide, and said cleavage agent under conditions such that a cleavage structure is formed from said target nucleic acid, said bridging oligonucleotide, and said second oligonucleotide, and wherein either said second oligonucleotide or said bridging oligonucleotide is cleaved by said cleavage agent.

C2 93. The method of Claim 92, wherein said thermostable 5' nuclease comprises a modified polymerase; wherein said modified polymerase is a modified native polymerase of *Thermus* species.

C3 101. A method, comprising:

(3)

- a) providing:
 - i) target nucleic acid comprising first and second non-contiguous single-stranded regions separated by an intervening region comprising a double-stranded portion, wherein said target nucleic acid comprises at least a portion of Hepatitis C virus nucleic acid;
 - ii) a bridging oligonucleotide capable of binding to said first and second non-contiguous single-stranded regions; and
 - iii) a reactant selected from the group consisting of polymerases and ligases; and
- b) mixing said target nucleic acid, said bridging oligonucleotide and said reactant under conditions such that said bridging oligonucleotide hybridizes to said target nucleic acid, and wherein said bridging oligonucleotide is modified by said reactant to produce a modified oligonucleotide.

(4)

111. The method of Claim 107, wherein either said first oligonucleotide or said second oligonucleotide comprises a fluorescent label and said detecting the cleavage of said cleavage structure comprises detection of fluorescence from said fluorescent label.

(5)

113. The method of Claim 107, wherein said first and second oligonucleotides collectively comprise a fluorescence energy donor and a fluorescence energy acceptor and wherein said detecting the cleavage of said cleavage structure comprises detection of fluorescence energy transfer between said fluorescence energy donor and said fluorescence energy acceptor.

(6)

114. The method of Claim 107, wherein said either said first oligonucleotide or said second oligonucleotide comprises a label selected from the group consisting of a radioactive label, a luminescent label, a phosphorescent label, a fluorescence polarization label, and charge label, and detecting the cleavage of said cleavage structure comprises detection selected from the group consisting of detection of radioactivity, luminescence, phosphorescence, fluorescence

(b) polarization, and charge from said label.

(c) 121. The method of Claim 120, wherein a portion of the amino acid sequence of said nuclease is homologous to a portion of the amino acid sequence of a thermostable DNA polymerase from a thermophilic organism.

(d) 123. The method of Claim 107, wherein said detecting the cleavage of said cleavage structure comprises:

a) providing:
i) said non-target cleavage product;
ii) a composition comprising two single-stranded nucleic acids annealed so as to define a single-stranded portion of a protein binding region; and
iii) a protein; and
b) contacting said non-target cleavage product and said single-stranded portion of said protein binding region under conditions such that said non-target cleavage product and said single-stranded portion of a protein binding region hybridize to form a double stranded protein binding region, and wherein said protein binds to said double stranded protein binding region.

124. The method of Claim 123, wherein said protein comprises a nucleic acid polymerase and wherein said nucleic acid polymerase binds to said protein binding region and produces nucleic acid.

(e) 127. The method of Claim 107, wherein said detecting the cleavage of said cleavage structure comprises:

a) providing:
i) said non-target cleavage product;
ii) a single continuous strand of nucleic acid comprising a sequence defining a single strand of an RNA polymerase binding region;

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- iii) a template-dependent DNA polymerase; and
- iv) a template-dependent RNA polymerase;
- b) contacting said non-target cleavage product and said RNA polymerase binding region under conditions such that said non-target cleavage product binds to a portion of said single strand of said RNA polymerase binding region to produce a bound non-target cleavage product;
- c) contacting said bound non-target cleavage product and said template-dependent DNA polymerase under conditions such that a double-stranded RNA polymerase binding region is produced; and
- d) contacting said double-stranded RNA polymerase binding region and said template-dependent RNA polymerase under conditions such that RNA transcripts are produced.

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136. The method of Claim 107, further comprising providing a third oligonucleotide complementary to a third portion of said target nucleic acid upstream of said first portion of said first target nucleic acid, wherein said third oligonucleotide is mixed with said reaction mixture in step b); and wherein said third oligonucleotide is annealed to said third portion of said target nucleic acid.

REMARKS

Claims 90-136 are pending. The Examiner has rejected Claims 90-98 under the judicially created doctrine of obviousness-type double patenting as being unpatentable over claims 1-7 of U.S. Patent 6,194,149. The Examiner has also rejected Claims 99-100 under the judicially created doctrine of obviousness-type double patenting as being unpatentable over claim 1 of U.S. Patent 6,355,437. The Examiner has further rejected Claims 101-106 under the judicially created doctrine of obviousness-type double patenting as being unpatentable over claim 1 of U.S. Patent 6,355,437 in view of U.S. Patent 6,194,149. Applicants respectfully disagree with this rejection. Nonetheless, the Applicants submit herewith a terminal disclaimer in compliance with 37 CFR 1.321 (c).

The Applicants submit herewith a form PTO-1449, an Information Disclosure Statement